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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,865	10/06/2003	Usha Kasid	224382	8115
23460	7590	09/23/2005		
LEYDIG VOIT & MAYER, LTD TWO PRUDENTIAL PLAZA, SUITE 4900 180 NORTH STETSON AVENUE CHICAGO, IL 60601-6780				
			EXAMINER AEDER, SEAN E	
			ART UNIT 1642	PAPER NUMBER

DATE MAILED: 09/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/679,865

Applicant(s)

KASID ET AL.

Examiner

Sean E. Aeder, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 May 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-8,10,13,14,16,19,20 and 36-54 is/are pending in the application.
- 4a) Of the above claim(s) 13,14,16,19,20,40,41 and 44-54 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-8,10,36-39,42 and 43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 06 October 2003 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____

- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

Detailed Action

The Election filed 8/12/05 in response to the Office Action of 5/31/05 is acknowledged and has been entered. Applicant elected group I with traverse.

The traversal is on the ground(s) that the claims of groups II-X are dependant on the claims of group I, and thus include the subject matter of group I. Moreover, Applicant asserts that the currently presented claims link each of the separate groups identified in the office action to group I. Applicant further asserts that upon allowance of a linking claim, the restriction requirement must be withdrawn pursuant to MPEP 809.03. This is not found persuasive. Claims of group I are not "linking claims" to claims of any other group. "Linking claims" complicate restriction by linking inventions that are otherwise divisible (see MPEP 809.03). Claims 13-14 and 16, for example, are drawn to polypeptides that are encoded by the nucleic acid sequences of group I; *however*, these claims are not linked to group I as the polypeptide invention is easily divisible from the nucleotide invention of group I. Further, MPEP 802.01 provides that restriction is proper between inventions which are independent or distinct. Here, the inventions of the various groups are distinct for the reasons set forth in the Office Action. Each of the groups outlined in the restriction include distinct nucleotide sequences, distinct polypeptide sequences, distinct antibodies, distinct agents, distinct methods of inhibiting apoptosis or proliferation, distinct methods of treating cancer, and distinct methods of detecting cancer. Each of these inventions is further unrelated as they comprise distinct steps and utilize different products which demonstrates that each

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method has a different mode of operation. Searching and examining each of these products and methods would result in a serious burden on the examiner. Furthermore, it is noted that the literature search, particularly relevant in this art, is not coextensive and is very important in evaluating the burden of search. Different searches and issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Newly submitted claims 44-54 are directed to inventions independent or distinct from the elected invention, therefore claims 44-54 will not be examined with elected group I. Group I is drawn to a polynucleotide sequence, while claims 44-54 are drawn to distinct methods. Examining a product invention with both screening and treating methods would impose a serious search burden on the examiner. Accordingly, claims 44-54 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Further, newly added claims 36-39, 42 and 43 will only be examined to the invention drawn to a polynucleotide sequence and not inventions drawn to ribozymes or other agents (see claims 36-37).

Claims 1, 2, 4-8, 10, 13, 14, 16, 19, 20, and 36-54 are pending.

Claims 13, 14, 16, 19, 20, 40-41, and 44-54 are withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to a non-elected invention.

Claims 1, 2, 4-8, 10, and 36-39, 42, and 43 are currently under consideration.

Claim Objections

Claim 6 is objected to for reciting "...said polynucleotide has an amino acid sequence..." Polynucleotides do not "have" amino acid sequences. Polynucleotides "encode" amino acid sequences. Appropriate correction is required.

Claim 10 is objected to for reciting "... comprising the recombinant vector of claim 8 and a host cell." Interpreted broadly, Applicant is claiming the non-statutory subject matter of non-recombinant host cells. Claim 10 could also be interpreted to claim a host cell comprising a cell. Appropriate correction is required.

Claims 36-37 are objected to for reciting claims drawn to non-elected inventions. Claims should be amended so they are only drawn to the elected invention of polynucleotides.

Claims 36-39, 42, and 43 are objected to for being dependant upon non-elected claims. Appropriate correction is required.

Drawings

The drawings are objected to because the labeling of Figures 4 and 5 are unclear. In Figure 4, it is unclear which bands correspond with BRCC2 mRNA and

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which bands correspond with GADPH mRNA. In Figure 5, it is unclear which bands correspond with BRCC2 and which correspond with β -Actin. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 1-2, 4-8, 10, 36-39 and 42-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

The claims are broadly drawn to nucleic acids, vectors comprising said nucleic acids, and host cells comprising said vectors. The claims are further drawn to antisense oligonucleotides that inhibit the expression of said nucleic acids. However, the claims are not enabled because there is insufficient guidance and objective evidence that one

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of ordinary skill in the art would know how to predictably use the claimed invention. The specification teaches uses for the claimed polynucleotide that rely on the assertion that BRCC2 is involved in a raf-1 apoptotic pathway. These uses include gene therapy (paragraph 92, in particular).

The specification alleges that BRCC2 is involved in an apoptosis pathway since expression of BRCC2 is decreased and apoptosis is increased upon antisense-raf treatment of MDA-MB cells (paragraph 32, in particular). Applicants suggest that a concomitant decrease in BRCC2 expression upon inhibition of Raf1 expression demonstrates that BRCC2 and Raf1 are both involved in signaling pathways controlling apoptosis (paragraphs 32 and 33, in particular). However, Bennett et al. (Circulation, 1995, 92(7):1981-1993) teaches that though antisense technology has been instrumental as a tool for helping delineate signaling pathways controlling various cellular functions, the questionable specificity of antisense constructs requires control measures to be performed in order for effects to be attributed solely to the decrease of expression of a particular gene (see page 1987, in particular). The most convincing controls are those that use overexpression of the target mRNA or more directly add back the protein to counter the effects of the antisense oligonucleotide (page 1987 right column, in particular). If the effects of the antisense can be reversed, then this is good evidence that the antisense oligonucleotide has acted by specific hybridization to the target mRNA. In

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addition, good evidence of specific hybridization is provided by an observation that multiple oligonucleotides to the same target mRNA induce a similar biological effect, because it is unlikely that oligonucleotides of very different sequence would have similar secondary targets (page 1987 right column, in particular). *However*, employing these controls with antisense Raf-1 constructs would only indicate whether Raf-1 expression controls BRCC2 expression and would *not* indicate whether BRCC2 is involved in apoptosis as those skilled in the art would recognize that Raf-1 could be involved in divergent signaling pathways that mediate completely different physiological processes. Those of skill in the art would recognize that demonstrating an increase in apoptosis upon direct inhibition of BRCC2 expression by antisense-BRCC2 constructs with the proper controls would obviate this rejection. Thus, Applicant is not enabled to use BRCC2 polynucleotides to modulate apoptosis as disclosed in the specification.

Claims 1, 2, 4-8 and 10 are further rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the written description is not commensurate in scope with the claims drawn to the genus of polynucleotides comprising sequences less than 100% identical to SEQ ID NO:1 that

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encode the polypeptide of SEQ ID NO:2 ("90% identical", polynucleotide complements, random contiguous nucleotides, substitutions, additions, deletions, random compliment sequences). This is a **written description rejection**.

Some of the factual considerations that are weighed when determining a written description include the level of skill and knowledge in the art, the disclosure of complete or partial structures, the disclosure of physical and or chemical properties, adequate disclosure of the functional characteristics, the correlation between structure and function, and disclosure of methods of making.

The claims do not require that the polynucleotides possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polynucleotides that is defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. Further, there is no identification

of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF’s were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 4-7, and 36-39 are rejected under 35 U.S.C. 102(a) as being anticipated by Birren et al. (Homo sapiens chromosome 11 clone RP11-85D24 map 11, 4/22/00, see attached).

Birren et al. teach an isolated nucleic acid molecule comprising a polynucleotide that is >99% identical to a polynucleotide encoding amino acids 1 to 108 of the amino acid sequence contained in SEQ ID NO:2. The nucleic acid molecule taught by Birren et al. is also comprised of about 2 to about 324 contiguous nucleotides from the nucleotide sequence of SEQ ID NO:1. The nucleic acid molecule taught by Birren et al. is also comprised of a polynucleotide wherein, except for a single conservative amino acid substitution, said polynucleotide has an amino acid sequence of amino acids from 1 to 108 of the amino acids sequence in SEQ ID NO:2. Further, antisense

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oligonucleotides to the sequences described above are anticipated by the sense sequence taught by Birren et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4-8 and 10 are also rejected under 35 U.S.C. 103(a) as being unpatentable over Birren et al. (Homo sapiens chromosome 11 clone RP11-85D24 map 11, 4/22/00, see attached).

Birren et al. teach an isolated nucleic acid molecule comprising a polynucleotide that is >99% identical to a polynucleotide encoding amino acids 1 to 108 of the amino acid sequence contained in SEQ ID NO:2. The nucleic acid molecule taught by Birren et al. is also comprised of 2 to 324 contiguous nucleotides from the nucleotide sequence of SEQ ID NO:1. The nucleic acid molecule taught by Birren et al. is also comprised of a polynucleotide wherein, except for a single conservative amino acid substitution, said polynucleotide has an amino acid sequence of amino acids from 1 to 108 of the amino acids sequence in SEQ ID NO:2. Further, antisense oligonucleotides to the sequences described above are anticipated by the sense sequence taught by Birren et al.

Birren et al. does not *specifically* teach a recombinant vector comprising the nucleic acid molecule comprising a polynucleotide that is >99% identical to a polynucleotide encoding amino acids 1 to 108 of the amino acid sequence contained in SEQ ID NO:2 (claim 8) or a recombinant host cell comprising this vector (claim 10). However, these deficiencies are rendered obvious.

When cloning a novel polynucleotide, it is obvious to clone the polynucleotide into a recombinant vector and introduce said vector into a host cell in order to produce recombinant nucleic acids and proteins for subsequent functional studies. An example of cloning polynucleotides into recombinant vectors and introducing said vectors into host cells for subsequent functional studies is taught by Eriksson et al. (U.S. Patent

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5,928,939, 7/27/99). Eriksson et al. teaches the cloning of a polynucleotide encoding vascular endothelial growth factor-B into a vector and introduction of said vector into a host cell in order to produce recombinant nucleic acids and proteins to study cell proliferation (see examples 9 and 10, in particular)

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to clone the polynucleotide into a recombinant vector and introduce said vector into a host cell and incorporate antisense constructs into liposomal formulations. Further, one would have been motivated to do so because host cells comprised of vectors expressing a gene of interest allow production of recombinant amino acids and proteins for functional studies and antisense constructs incorporated into liposomal formulations enhance the ability of the constructs to enter target cells. Further, one of skill in the art would have a reasonable expectation of success in producing the claimed vectors, recombinant cells, and liposomal constructs since these methods are well known and conventional in the art.

Summary

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SEA



**GARY B. NICKOL, PH.D.
PRIMARY EXAMINER**